REMARKS

Claims 1, 4, 7, 14 and 57-58 are pending. The support for the amendments to claim 1 are found in claim 1. No new matter is added.

The Applicant appreciates the Examiner's time during the telephone discussion on January 4, 2010.

Claims 1 and 4 stand, and Claim 57 is newly rejected under 35 U.S.C. 103(a) as being unpatentable over Mejia et al (Genomics 70(2):165-170, 2000; *of record in IDS, AE), in view of Perkins et al (US 2003/0119104 Al), Waye et al (Mol. and Cell. Biol. 6(9):3156-3165, 1986) and Ikeno et al (Human Mol. Gen. 3(8):1245-1257, 1994; *of record in IDS, CE). (Office Action, page 3)

The method now claimed is clearly different from the combination of the cited art for several reasons including the following:

First, Mejia uses two kinds of vectors (referred to as vectors A and B for convenience of explanation). These two vectors are ligated *in vitro* using *E. coli*. Then, thus obtained construct (A + B) is introduced into a host cell to construct a HAC. Therefore, the material for HAC in the method of Mejia is only one construct and the HAC constructed by this method inevitably has a structure that vectors A and B are arranged alternately (--A-B-A-B-A-B--). This is shown in FIGS. 2 and 3 of Mejia.

In contrast, the claimed method introduces two vectors (referred to as vectors A and B for convenience of explanation) to construct a HAC. Namely, unlike Mejia, only one step is used to construct a HAC in the claimed method. As a result of this step, various kinds of HAC (e.g. --AAAAA-B-AAAA--; --AA-B-AA-B-AA--; and –AA-BB-A-B-AA--) are constructed, which makes it possible to select a desirable HAC according to need. In this regard, the claimed method is far more versatile and has much more practical value than Mejia. As explained in the published specification (emphasis added):

> [0159] By adjusting the ratio of the first vector including a mammalian centromere sequence and the second vector including the inserting sequence as a functional sequence, ***it is possible to change the number of inserting sequences incorporated into a mammalian artificial chromosome to be produced.***

> Furthermore, when the mammalian artificial chromosome is produced by the co-introduction of such first vector and second vector, it is possible to incorporate the inserting sequence at a distance from a centromere (i.e. location which is not between centromere) in a mammalian artificial chromosome to be produced, so that a mammalian artificial chromosome that holds an insertion sequence functioning appropriately can be constructed.
>
> [0161] Concrete examples of the mammalian artificial chromosome precursor (second vector) used in the case where the insulator sequence is used include one having an inserting sequence of loxP etc. as a functional sequence and having an insulator sequence at the 5' side of the inserting sequence can be used.
>
> [0162] In the mammalian artificial chromosome precursor (second vector), an insulator sequence may be disposed at 3' side instead of 5' site of the inserting sequence. Alternatively, a mammalian artificial chromosome precursor (second vector) in which insulator sequences are disposed at both sides so that they sandwich the inserting sequence. ***Furthermore, when an insulator sequence is disposed at any positions, a plurality of insulator sequences may be continuously disposed or may be disposed with other sequence interposed therebetween.***

In the meantime, according to common knowledge in this art, a HAC should have a structure that vectors are ligated repeatedly several times or some dozen times as a certain length is required to form a functional HAC. Therefore, the very limited method of Mejia cannot construct a HAC in which only one of vector B is contained, whereas the claimed method can.

Apparently, the above decisive differences between the claimed invention (HAC is constructed from two vectors by **one step**) and Mejia (HAC is constructed from two vectors by **two steps**) cannot be cured by Perkins, which merely teaches using a mammalian host cell.

As apparent from the specification, the insertion sequence is provided from the second vector, which is one of the features of the claimed method. The insertion sequence is not for a ligation of the two vectors.

Regarding the method steps, the second and third steps are both necessary. The second step is a step to select/identify transformants. The third step serves as a step to select/identify cells which contain a HAC constructed by ligation of the two vectors among the tranformants. As explained in the specification (emphasis added):

> [0169] ***After the first vector and the second vector are introduced, transformed cells (transformants) are selected (second step).*** The selection of the transformed cells can be carried out by selectively culturing the cells after introduction of the vectors by using the selection marker gene which was inserted in the first vector or second vector in advance. Note here that as a result of isolating cells arbitrarily from the cell group to which both vectors were introduced, the isolation operation in the case where the isolated cells are transformed cells is encompassed in the "selection of transformed cells" according to the present invention.
>
> [0170] ***After the transformed cells are selected, a cell containing a MAC is selected (third step).*** Such a selection operation can be carried out by a detection method using a probe or antibody specific to MAC. ...

In short none of Mejia, Perkins, Wayne or Ikeno discloses the method now claimed, nor does the combination of references suggest the claimed invention. It is therefore respectfully requested that the rejection be reconsidered and withdrawn.

Claim 7 stands rejected under 35 U.S.C. 103(a) as being unpatentable over Mejia et al (Genomics 70(2):165-170, 2000; *of record in IDS, AE), in further view of Waye et al (Mol. and Cell. Biol. 6(9):3156-3165, 1986), Ikeno et al (Human Mol. Gen. 3(8):1245-1257, 1994; *of record in IDS, CE) and Perkins et al (US 2003/0119104 Al), as applied to claims 1, 4 and 57 above, and in further view of Bokkelen et al (U.S. Patent No. 5,695,967). (Office Action, page 3)

The addition of Bokkelen does not compensate for the deficiencies of Mejia, Wayne, Ikeno, and Perkins. As a result a *prima facie* rejection of obviousness cannot be maintained over the invention now claimed.

It is respectfully requested that the rejection be reconsidered and withdrawn.

Claim 14 stands rejected under 35 U.S.C. 103(a) as being unpatentable over Mejia et al (Genomics 70(2):165-170, 2000; *of record in IDS, AE), in further view of Waye et al (Mol. and Cell. Biol. 6(9):3156-3165, 1986), Ikeno et al (Human Mol. Gen. 3(8):1245-1257, 1994; *of record in IDS, CE), Perkins et al (US 2003/0119104 Al) and Bokkelen et al (U.S. Patent No. 5,695,967), as applied to claims 1, 4, 7 and 57 above, and in further view of Cooke et al (WO 00/18941). (Office Action, page 3)

The addition of Cooke does not cure the deficiencies of the combination of Mejia, Wayne, Ikeno, Perkins and Bokkelen. As a result a *prima facie* rejection of obviousness cannot be maintained over the invention now claimed.

It is respectfully requested that the rejection be reconsidered and withdrawn.

Claim 58 is rejected under 35 U.S.C. 103(a) as being unpatentable over Mejia et al (Genomics 70(2):165-170, 2000; *of record in IDS, AE), in further view of Waye et al (Mol. and Cell. Biol. 6(9):3156-3165, 1986), Ikeno et al (Human Mol. Gen. 3(8):1245-1257, 1994; *of record in IDS, CE), Perkins et al (US 2003/0119104 Al), Bokkelen et al (U.S. Patent No. 5,695,967) and Cooke et al (WO 00/18941), as applied to claims 1, 4, 7, 14 and 57 above, and in further view of Okazaki et al (WO 98/08964). (Office Action, page 4-5)

The addition of Okazaki does not cure the deficiencies of the combination of Mejia, Wayne, Ikeno, Perkins, Bokkelen and Cooke. As a result a *prima facie* rejection of obviousness cannot be maintained over the invention now claimed.

It is respectfully requested that the rejection be reconsidered and withdrawn.

In view of the above amendment, applicant believes the pending application is in condition for allowance.

The Director is hereby authorized to charge any deficiency in the fees filed, asserted to be filed or which should have been filed herewith (or with any paper hereafter filed in this application by this firm) to our Deposit Account No. 04-1105.

Dated: February 16, 2010

Respectfully submitted,

Customer No. 21874

Electronic signature: /James E. Armstrong, IV/
James E. Armstrong, IV
Registration No.: 42,266
EDWARDS ANGELL PALMER & DODGE LLP
P.O. Box 55874
Boston, Massachusetts 02205
(202) 478-7375
Attorneys/Agents For Applicant